CHAPTER 7 FUNDAMENTAL PHYSICS TECHNOLOGIES FOR EXPLORATION AND ASTRONAUT HEALTH

SQUID and Other Technologies

by Bob Silberg, Raytheon

James Adams of Marshall Space Flight Center discussed radiation hazards and countermeasures for human space flight. He posed the problem of understanding the effects of ionizing radiation on astronauts, and suggested such possible countermeasures as material and magnetic shielding, and operational and biological countermeasures. Regarding material shielding, he said that rather than attempt to stop heavy ions completely, the best strategy would be to break up heavy ions into light ions. Hydrogen would be best for this, since it would put a lot of target nucleons in the way.

Claudia Tesche of the University of New Mexico reported on the use of magnetoencephalography (MEG), applying superconducting instruments (SQUIDs) to detect magnetic fields generated in the brain, to explore psychological issues by correlating behavior with the observed neural activities Tesche also cautioned that since transcranial magnetic stimulation (TMS) stimulates the brain, caution needs to be exercised regarding the use of magnetic levitation.

JPL's Slava Turyshev gave an overview of the role of fundamental physics in human space exploration. He discussed new technologies and materials, radiation countermeasures, wearable computers and EVA suits, and sensors and devices for life support. He described carbon nanotubes as an advanced material that could be of great use within five to seven years.

Talso Chui, also of JPL, spoke of the development of flight SQUIDs for applications in planetary exploration. He said the SQUID is the lowest-noise preamplifier available, about 100 times better than the transistor. It is noninvasive and is not affected by insulating tissues and bones, which gives it an advantage over electrical signals in medical imaging. He concluded that the flight SQUID development program for fundamental research on the ISS can be redirected to address human health issues related to space travel, and that a mini-MRI stands out to be most suitable for space flight. It may be possible to design a modular demountable SQUID unit for multiple functions related to space exploration.

Michael Romalis of Princeton University said that his team has developed a high-sensitivity and high-spatial-resolution atomic magnetometer based on measurement of the Larmour frequencies of gaseous atoms. This atomic magnetometer provides an alternative to the SQUID for diagnostics and medical monitoring in space, with the advantage of not requiring superconductors or bulky dewars for cryogenic cooling.

Virendra Sarohia of JPL called for adoption of principles found in biological systems to improve engineering of autonomous systems for space exploration. He said that bio-engineered systems could substitute information for spacecraft mass to greatly decrease mission launch cost. He spoke of human-machine partnerships, closed ecosystem management, artificial neural networks, nanoscale fluid mechanics, self-healing systems (such as self-correcting integrated circuits), and the redesign of microbes to detect and remedy chemical/environmental problems.

Ron Walsworth of the Smithsonian Astrophysical Observatory spoke about designing a low-field MRI instrument using spin-polarized noble gas NMR. Such technology, which is useful for noninvasive biomedical imaging of the lungs in action, would also be good for monitoring astronauts, and for NMR probes of porous and granular media (rocks of the Moon and Mars, for example). He said this has interest from NASA's bioastronautics program, and observed that many of the things that interest fundamental physicists are, with a little twist, also of interest to the Moon/Mars program.

Radiation Hazards and Countermeasures for Human Space Flight

James Adams
Marshall Space Flight Center

The protection of astronauts from the hazards of ionizing radiation in space is a moral and legal obligation of NASA. If there are to be manned deep-space missions, means must be found to provide this protection. There are two parts to providing this protection: understanding the effects of space radiation on humans so that radiation exposure limits can be established; and developing countermeasures so that exposures can be kept below these limits. This talk will cover both parts of this problem.

Using MEG to Explore Issues in Psychology

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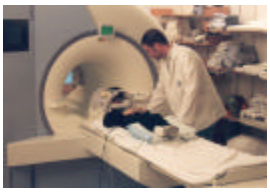
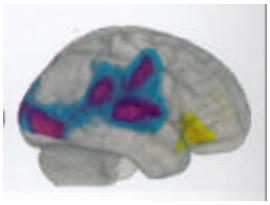
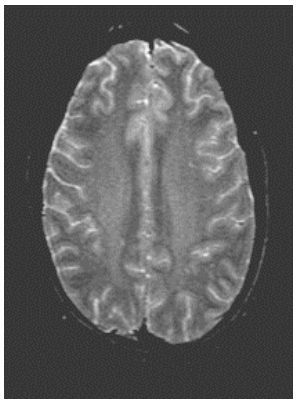
Psychology is the study of human behavior. Research in my laboratory in the Department of Psychology at UNM, and in many other laboratories dedicated to brain research, is motivated by the hypothesis that there is a biological basis for human behavior. We believe that human behavior is the product of ongoing processes in the brain and is thus constrained by and emerges from the structure, connectivity and function of specific brain structures.

We now have a remarkable set of tools that allow us to map the human brain in exquisite detail. We can image brain anatomy, chemistry and metabolism, and even monitor the dynamics of neuronal population activity from outside the head. The goal of non-invasive functional neuroimaging studies is to correlate observations of brain activity with behavior over the entire lifespan of the human nervous system, from several months before birth into old age. Measures of ongoing brain activity may provide a remarkable opportunity to both predict and control behavior. Finally, individuals who suffer from a wide variety of mental disorders display significant differences from normal subjects in both brain structure and function. Characterizing these differences aids in the diagnosis of disease and may also contribute to the evaluation of the efficacy of a wide variety of clinical interventions.

A partial list of neuroimaging methodologies includes magnetic resonance imaging (MRI), magnetic resonance spectroscopy (MRS), functional magnetic resonance imaging (fMRI), magnetoencephalography (MEG), electroencephalography (EEG) and transcranial magnetic stimulation (TMS). These tools are used by the community both separately and in various combinations. I will now describe each of these methods briefly, and then discuss in some detail the use of whole-scalp magnetoencephalography to image ongoing neuronal activity within the human brain.



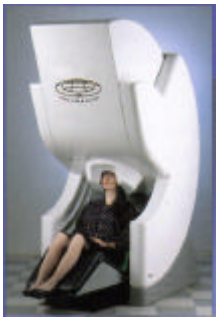




Structural information, including brain connectivity, is usually obtained through MRI. The signals are magnetic-field dependent radio frequency emissions from the nuclei of atoms. Structural MRIs provide a platform for integration of data across different imaging modalities.

MRS is performed with the same scanner used to perform MRI. MRS allows us to image the spatial distribution of chemical compounds within the brain that are of biological significance.

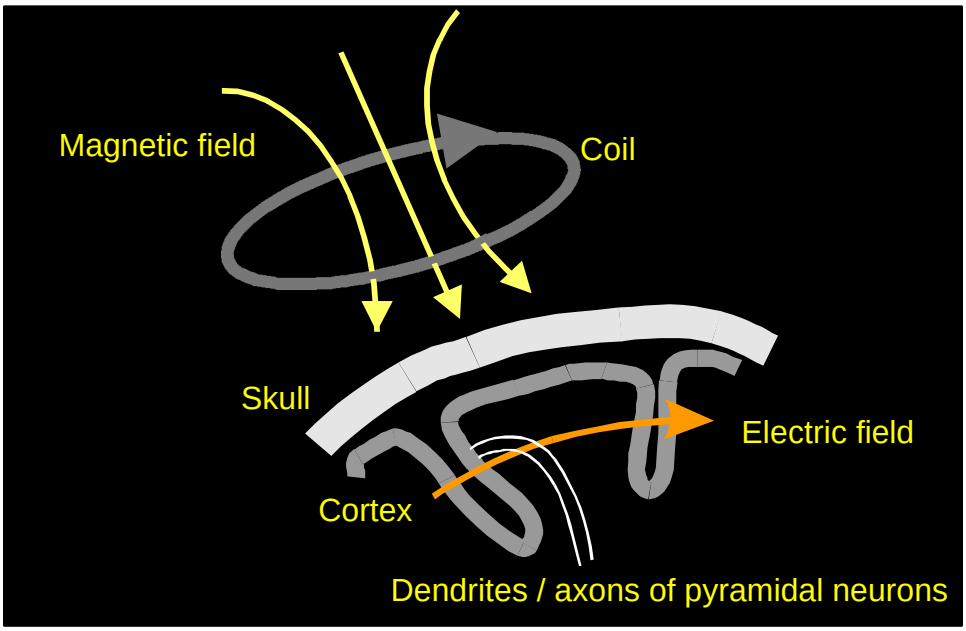
Functional MRI is a clever way to turn a metabolic artifact seen on MR images into a signal that correlates well with functional brain activation. The spatial resolution of this method is excellent, but the temporal resolution is limited to ~ 100 ms.



MEG and EEG are sister technologies. Both record the effects of current flow in the brain, and thus are a direct measure of neuronal activity. The image at the left shows a commercial MEG array of 306 DC SQUID (Superconducting Quantum Interference Device) sensors located in a cryogenic dewar (VectorView™, Elekta Neuromag, Ltd). The temporal resolution of both MEG and EEG is exquisite, on the order of milliseconds or better. The spatial resolution is ~0.5–1 cm, although there are some interesting issues associated with data inversion and interpretation.

Importantly, although fMRI, MEG, EEG, and to some extent, also MRS, can identify brain areas that are active during processing of sensory input or the performance of some task, none of these methods can prove that a given brain area is essential for a specific behavior. Being "on-line" for the reception of information is not necessarily the same as being 'in-line" and critical for the generation of a specific behavioral response.

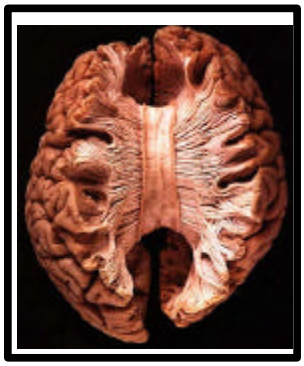
Lesions produced by either surgical, cryogenic or chemical methods have been used for many years to probe the criticality of specific brain structures to behavior in animal studies. Such research is impossible for ethical reasons in humans, although patients that present with lesions have provided invaluable information on the localization of function in the human brain. TMS provides a method for creating a temporary "functional lesion" in a brain structure or network in normal human subjects. If the application of a brief TMS pulse or train of pulses changes the subject's behavior, then we can be fairly certain that this area or network is an active player in that task.

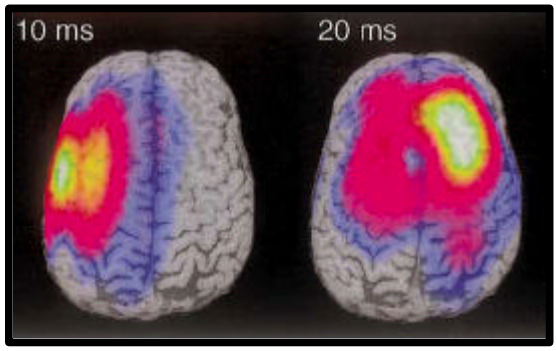


TMS and MEG are reciprocal methodologies. In TMS, a figure-of-eight coil located above the scalp is used to create changes in the magnetic field strength. External magnetic fields easily penetrate the skull. Thus changes in the current flow in the coil can be used to create time-dependent electric fields within superficial cerebral cortex. The induced electric field depolarizes cell membranes, and drives current flow within the dendrites of the cortical neurons. The

dendrites are branching, tree-like structures of nerve cells that receive inputs from other nerve cells. TMS can also stimulate the axons of nerve cells. These are the tracts that connect nerve cells to nearby or more distant target cells in the brain.

In MEG, the situation described above is reversed. Current flow in the dendrites of a local population of neurons generates a magnetic field that is linked into a pickup-coil located over the scalp. Changes in the magnetic flux threading the pickup loop are sensed by a DC SQUID detector located within a cryogenic dewar placed over the scalp.



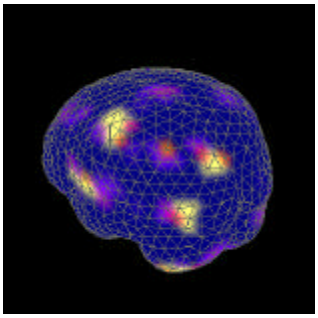


The images shown above illustrate a very important feature of brain organization. The cerebral cortex is a thin, convoluted sheet of neurons that covers the outer surface of the brain. Localized patches within cortex appear to do specific calculations. Some areas process visual input, other areas are associated with movement, and so forth. The various areas are connected together through axons that are bundled up into fiber tracts. On the left we see a beautiful image of the dissected brain viewed from above. The front of the head is at the top. The wrinkly cortical sheet on the left side of the brain is connected to the cortex on the right side through a thick bundle of axons: the corpus callosum. Can we use functional neuroimaging methods to image the consequence of this massive connection between the left and right hemispheres of the brain? Yes! On the right, we see contour maps of scalp EEG potentials recorded from a normal human subject (Ilmoniemi et al. 1997). The contour maps are visualized over 3-D rendering of MR images of the subject's cerebral cortex. The view is looking down at the brain from above the head. In this study, TMS has been used to activate a small patch of cortex on the left. Within 10 ms this activation has spread through the corpus callosum to the opposite hemisphere.

Take-home message: the brain is connected together in a very discrete and highly organized fashion. We need more than just a map of the locations of different processing centers. We need to understand the connections between different areas, and the dynamics, on a millisecond timescale, of the activation of all of the components of a vast number of functional brain networks.

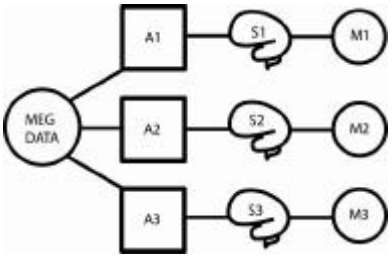
MEG provides a powerful tool for the observation of brain dynamics. Commercially available whole-scalp MEG systems now consist of ~100–300 DC SQUID magnetometers mounted into a cryogenic dewar. The SQUID sensors measure the very weak magnetic fields generated by current flow in the dendrites of neurons in the brain. There are approximately 60 such systems now in operation in clinical and research settings worldwide. Basic research is now underway using MEG arrays on a wide variety of different topics, including sensory processing, attention, working memory, language, executive function, emotional processing, classical conditioning, movement and temporal estimation. Clinical research studies include epilepsy, stroke, Parkinsons' disease, schizophrenia, autism and dyslexia. The main clinical applications are in the

functional localization of regions of cortex that are critical to vision, hearing, language and movement, and also the localization of areas that appear to initiate epileptic seizures. These epileptic foci may be removed either surgically or from outside the head with a gamma-knife.

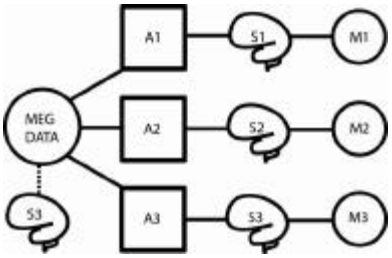


How is MEG used to map network phenomena in the normal human brain? We utilize an inversion algorithm to convert the signals from the SQUID detectors into current flow throughout the brain. The image at the left shows an example of current flow projected out onto a triangular mesh model of the surface of the brain. The view is of the back/left of the brain, with the front of the brain on the left. The regions of high activation, shown in yellow/red, are generated by brain processes supporting movements of the right index finger. These movements were cued by visual stimuli. Activity can be seen in the back of the brain in areas associated with visual processing, and also in the front of the brain in areas associated with the generation of movement.

Before we go any further, we must discuss an issue that complicates interpretation of both MEG and EEG data. Magnetic and electric signals recorded outside the head may be modeled by any one of an infinite number of current distributions within the brain. This is the so-called "inverse problem," although it really isn't a problem at all, but rather a statement of fact. The consequence of this ambiguity is that the community has spent a great deal of time inventing different inversion algorithms that convert MEG/EEG data into current distribution within the brain. The properties of these algorithms have been investigated through numerical simulations. However, numerical simulation cannot test the validity of the results of any given algorithm.



The flow chart on the left illustrates the use of numerical simulations to "check" a collection of inverse algorithms. Any given set of MEG data can be inverted using the algorithms A1–A3. Each of these generates solutions for current flow in the brain S1–S3. These solutions may be quite different. However, if the algorithms are implemented "correctly," then all the magnetic field patterns M1–M3 computed from each of the distributions should faithfully reproduce or approximate the original MEG data.



The flow chart on the left demonstrates that there is no way of determining the "correct" inversion algorithm from within the MEG data itself. If the actual current distribution used to generate the magnetic field pattern was S3, one of the algorithms (A3) may reproduce this distribution exactly. However all of the algorithms reproduce the measured MEG data.

We must also consider another, equally important problem, that of the tremendous complexity of the human brain. There are about 10^{11} neurons in the human brain. We can detect

MEG activity from a population of about 10^4. We need to address the limitations inherent in both the "inverse problem" and also in what looks like (and is!) a gross under-sampling of the data. As a result, any interpretation of MEG and/or EEG data must rest on a vast body of previous brain research, including information obtained from anatomical, lesion and other functional neuroimaging studies. The bottom line here is that the exercise of judgment in MEG/EEG data interpretation is unavoidable.

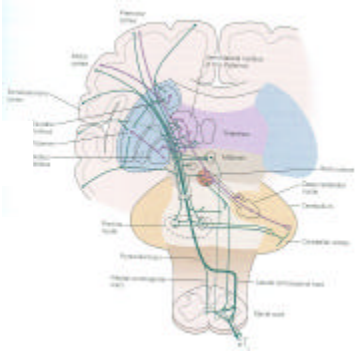
Take-home message: MEG/EEG are invaluable tools for exploring the dynamics of brain function, but cannot be used as "gold standard" methods. Verification of results requires other, more invasive methods.

What do we want to find out with MEG? We want to know how the brain works. Whole-scalp MEG arrays monitor ongoing activity all over the brain. Thus they are excellent tools for asking "big picture" questions about processes that may involve activation of very distributed brain networks. So lets ask a "big picture" question. How does the brain process information? Is there a "bottom up" flow of information from primary sensory receiving areas to higher order association areas where information is linked together, and then on to memory areas, where there is a comparison of the present input with past experiences, and then flow into some decision-making area, and finally activation of movement preparation and execution? This widely held "assembly-line" view of the brain views brain processing as serial, initiated by sensory input.

A slightly more elaborate, but still "bottom-up" model is that sensory input is divided up into components (color, shape, texture, aroma, etc.) and these components are processed in parallel. Parallel processing can dramatically increase the speed at which the rather leisurely brain, clicking along at several to tens of milliseconds per calculation, can conduct feed-forward analysis.

A very different model is that the brain has a life of its own. We think, and therefore we are. Information flows primarily from the "top" down, from executive and memory areas to sensory receiving areas. We look for what we expect, and want, to see. Introspection supports a "top-down" model, but of course, we want to see the grinding of neuronal gears that might make all this possible.

The final, and most likely, possibility is that the brain may function through a complex combination of all of the above.



What help can anatomy provide to resolve this issue? Here is a simplified example of the layout and wiring of the motor system. We can see feed-forward connections, feedback connections and also numerous possibility for feed-forward and feedback loops. Interestingly, there are typically 10 feedback connections for every 1 feed-forward connection. This observation alone supports that top-down and/or network models should be given serious consideration.

How about functional complexity? Numerous PET and fMRI studies demonstrate that even fairly simple cognitive tasks, such as attending to "when" vs. "where" an event is happening, elicit activation of multiple brain areas. Thus evidence is beginning to accumulate that favors the

view that the human brain undergoes complex, ongoing activity within multiple, interconnected and interacting cortical and subcortical networks. This ongoing activity is functional, and is gently modulated by, and affects, processing of sensory input.

Take-home message: Our goal will be to use MEG to parse out and explore the dynamics of brain networks that support ongoing functional activity.

Now I need to explain just a bit about our methods. I mentioned that we have an issue with the "inverse problem." Here is how we invert MEG scalp magnetic field signals into current flow in the brain. We use a minimum current estimate (MCE) algorithm (Uutela et al. 1999). We first make a boundary-element model for the conducting volume of the brain, including all cortical and subcortical structures. This model is used to solve the "forward problem," checking that the magnetic field that results from any one of many possible current distributions really matches our data. We then select the current distribution with the minimum total amplitude. The MCE inversion captures small transients in the data, as well as sustained and oscillatory activity within multiple brain areas.

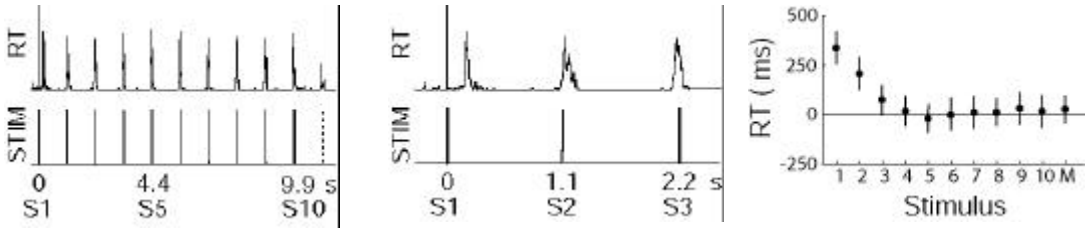
In my lab, we are now analyzing data from a 306-channel whole-scalp MEG array (VectorView™, Elekta Neuromag Ltd., located at the Helsinki University Central Hospital) with MCE inversion to study a wide variety of topics, including sensory processing, attention, working memory, associative learning, and generation of cued movement. I will discuss results from one study here (Tesche et al. 2004). Five subjects performed a very simple task under the MEG array. Each subject saw a train of letters ("O") presented one after another on a screen. The duration of each letter was 750 ms, with a 350 ms pause between letters, and the number of letters in each train was 10. There was a pause of 4.25 s between each train. The subjects were supposed to lift their dominant index finger every time they saw a letter, and relax it when the cue disappeared. They "keep time" with the visual cues.

Now, this doesn't sound very cognitive compared to a study that might probe, for example, some kind of memory process. Let me describe a typical task that might probe working memory. Working memory is what allows us to do complex calculations. We are able to hold several bits of information in mind long enough to be able to manipulate and combine the components into new information. Working memory, when driven by the experimentalist, requires attention to presented stimuli, a short-term memory store, the capacity to manipulate the stored information (or at least, to follow our instructions), and finally generation of some behavioral response that we can measure. I might ask you to take all the numbers you see on a computer screen and add them together. If the number is even, cheer. If the number is odd, don't.

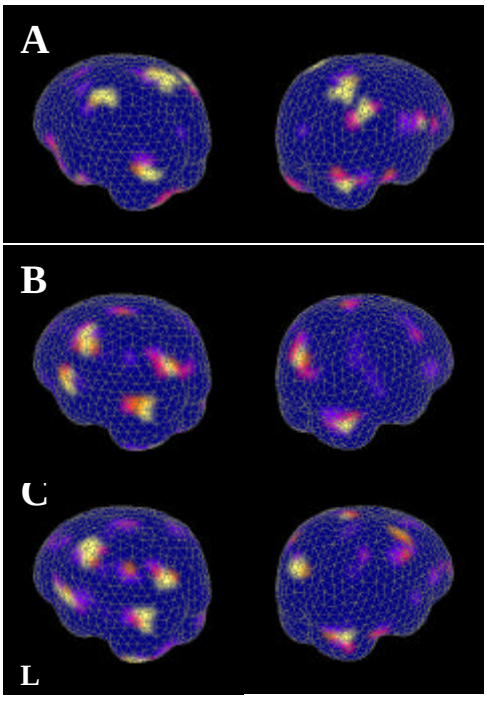
What does our cued movement paradigm have to do with working memory? Many working memory tasks present information with a fixed or predictable temporal pattern. As a result, task performance may involve attention to and memory of the temporal pattern of the presented stimuli, as well as the information content. More importantly our performance on many externally defined tasks improves when we can predict what might happen next. In fact, one might argue that the primary function of the human brain is predicting the future and deciding what to do about it.

Take-home message: The big question we are after here is: What brain networks mediate utilization of the capacity to predict future events? How do we learn to extract information about temporal patterns present in external stimuli and use that information to guide behavior?

Here are plots of the behavioral data for a single subject recorded during performance of the cued movement paradigm. The distribution of response times (RT) for each stimulus in the trains of ten stimuli show changes in the response time distributions with stimulus ordinal number. The subject reacts to the first stimulus S1 (the movements follow the cue), but begins to move in anticipation of subsequent cues. The response time distributions begin to shift in time and broaden until the finger movements are synchronized with the presentation of the cues, although with quite a bit of variance.



We looked at the MEG data in two ways. We were interested in brain activity that was time-locked with the presentation of the visual cues, and also activity that was time-locked with the finger lifts. We used MCE to image current flow in both cases. We were particularly interested in what happens during early learning, at about the 2nd cue in the train, and also what happens after they really get the hang of it, at about the 5th cue.



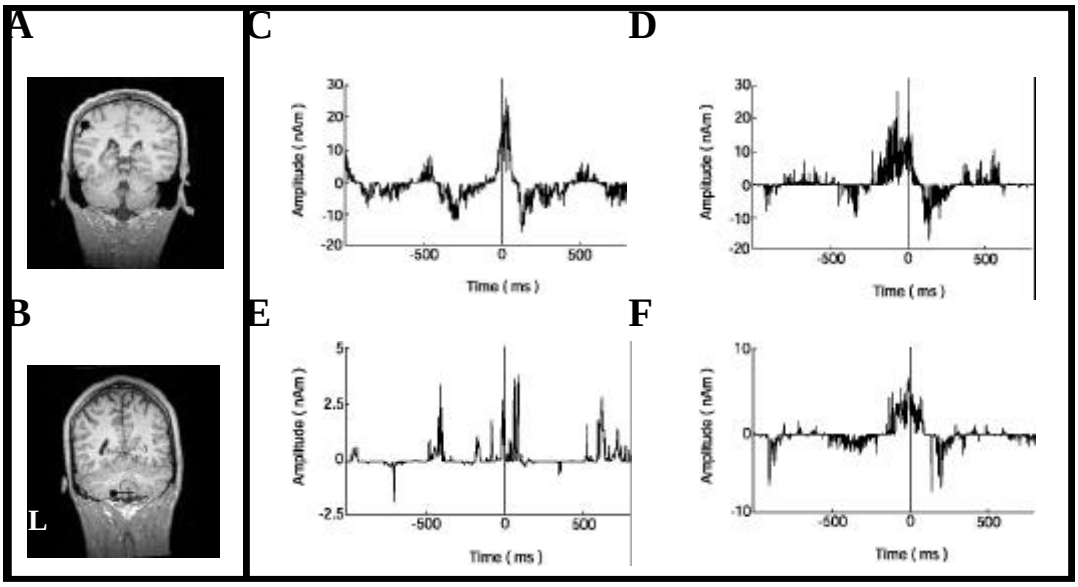
This is a snapshot of what's going on in a window of 20 ms centered on the 2nd cue.

This is a snapshot of what's going on in a window of 20 ms centered on the 4th + 6th cues.

This is a snapshot of what's going on in a window of 20 ms centered on the 4th – 6th movements.

The images A and B suggest that we have captured a dynamic shift in the location of the activated brain areas as this subject learns to produce anticipatory movement. Interestingly, the rather striking similarities between the MCE images B and C, for activity time-locked with cue

presentation and movement respectively, are most likely a result of the mean RT being nearly coincident with cue presentation for the 4^{th} – 6^{th} cues.

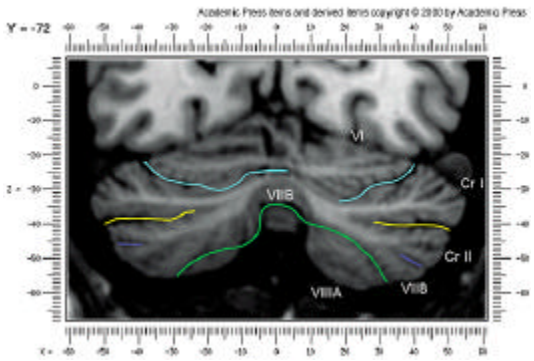


We used the MCE inversions to select out volumes of activation (VOA) in left somatomotor cortex (A) and in left inferior cerebellum (B). We approximated activity in these VOAs with current dipoles and imaged these dipoles onto the subject's MR images. The waveforms C– F show how these areas behave in time for different conditions. Responses time-locked with the 4^{th} – 6^{th} movements in left somatomotor cortex (C) are prominent immediately after the finger movements at t = 0. There is also quite a bit of activity throughout the epoch. Responses time-locked with the 4^{th} – 6^{th} movements in left inferior cerebellum (D) are prominent prior to and following movement. Interestingly, this same source in the left inferior cerebellum shows activity that is time-locked with the presentation of the 2^{nd} (E) and also the 4^{th} – 6^{th} (F) visual cues.

Why is it interesting to examine the inversion for activity in the cerebellum? About half of the neurons in the human brain are in the cerebellum. Remarkably, this structure has increased relative to the entire volume of the brain more than any other brain area, including our famous frontal cortex. Cerebellum is widely believed to be a "motor organ" and to participate to motor learning (Holmes 1939; Doyon et al. 1997; Doyon et al. 2002). Do human motor skills really require this much dedicated computing power compared to the other primates? There is now quite a bit of functional neuroimaging data that show cerebellar activation during a wide variety of cognitive tasks also (for a review, see Schmahmann 1997). Since the cerebellar cortex is very self-similar in structure, there is probably some core function or functions that this region is performing that involves cerebellum in a large number of different brain functions. There is quite a bit of controversy over what this function(s) might be, however.

Take-home message: Why is it especially interesting to observe cerebellar activity in the present context? Living in a low-gravity environment may be expected to induce significant cerebellar plasticity. The astronauts must adapt twice: once to learn motor skills appropriate to a space-based environment; and second, to learn or relearn skills appropriate to Earth. Interestingly, the cerebellar cortex is very self-similar, contains massive connections that link large regions of cortex, and demonstrates a fundamental form of brain plasticity. It is reasonable to consider that some changes in cognitive functions that involve the cerebellum might also accompany prolonged absence from an Earth-based environment.

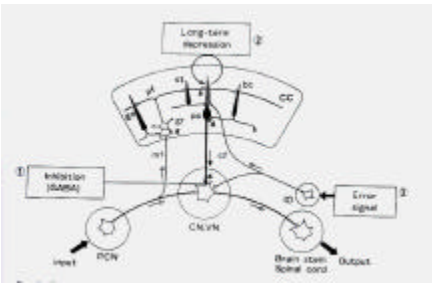
Thus it may be quite useful to develop simple paradigms and methods to interrogate cerebellar function.



At this point, some members of the MEG community might be thinking, "Wait a minute! It's impossible to see MEG/EEG signals from the cerebellum." The reason for their concern is that the cerebellar cortex is highly foliated, or wrinkly, on a rather fine scale. If there is current flow within a patch of cerebellar cortex that includes cortex from both sides of a fissure, the magnetic fields from individual dipoles on each side will tend to cancel out. We will be left with a very complex external field pattern that falls off rapidly with distance (Figure from Schmahman 1997).

However, the figure above shows that the cerebellar cortex also has very deep fissures. These fissures, and the structure of the individual folia, both break any symmetry in the current flow that would lead to complete cancellation of the external magnetic field. The magnetic fields from flattened cerebellar cortex are very large (Okada & Nicholson 1988). Thus we are actually well positioned to see cerebellum with MEG. Would it be possible to detect the cerebellum with EEG? This would be much more convenient, especially for a space-based system. Although the traditional answer is NO, this question has not been fully explored using modern inversion methods.

What does our data tell us about the role of the cerebellum? Does it participate in processing of sensory input or modulate motor output? We have seen evidence for both. Is it involved primarily in timing, or perhaps in attention or working memory? A very general model for the cerebellum that has the potential to involve this structure in a wide variety of cognitive functions is that the cerebellum participates to adaptive control (Ito 1994; Thach et al. 1992; Ito 1993). In this model, the cerebellum utilizes a prediction for future sensory input that results from a given movement for the construction of a comparison with ongoing sensory input. Discrepancies, or error signals, between the two are used to modulate the ongoing movement. However, the capacity to predict future sensory input may be useful for more than just tweaking the coordination of multiple muscle groups. Higher order brain function also involves coordination between multiple brain areas. Tweaking cognition may prove to be very similar to tweaking the action of multiple muscle groups. Finally, we suggest that the abstraction of a capacity to predict sensory input that accompanies movement to the prediction of future events, either internal or external, may be the "core" cerebellar function.

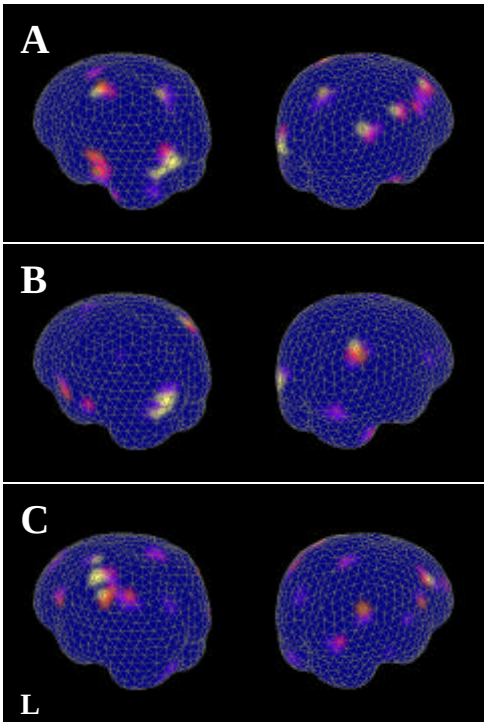


The wiring diagram of the cerebellum is unusually simple. There are two inputs to the cerebellar cortex: the mossy fibers; and the climbing fibers. There is a single output channel: from the Purkinje cells to the deep nuclei. We are most interested in the climbing fiber input to cerebellar cortex. This input originates in a brainstem nucleus called the inferior olive and is believed to represent error signals in the adaptive control model (Figure from Schmahmann 1997).

One of the great advantages of MEG is that we can observe, using non-invasive methods, oscillatory activity in the human cerebellum. The cerebellum is known to support two characteristic frequency bands of oscillatory activity. The characteristic frequency for inferior olivary input is about 6–10 Hz and for the mossy fiber input at about 25–45 Hz (Llinas and Yarom 1986). We have already demonstrated that MEG may be able to observe changes in the oscillatory component of cerebellar activity following stimulation of nerves in the wrist and fingers at both of these frequency bands (Tesche & Karhu 2000).

Why do we care about these oscillations? There is growing evidence that rhythmic activity may help to form transient functional links between different brain areas (Eckhorn et al. 1988; Gray & Singer 1989). Is the cerebellum part of this "orchestra of the brain"? Is it linked with other brain areas through oscillations? Can we see changes in shared oscillations that depend on what the subject is doing, or learning how to do?

We used the MEG data recorded during visually cued movement to investigate these issues. The subjects were learning how to synchronize finger movements to letters flashing on the computer screen. We extracted waveforms for somatomotor cortex, the area of the brain that gives motor commands and receives immediate feedback sensations from the skin and joints of the finger and hand. We then computed the semicoherence spectra between waveforms for this area and all the MEG sensor channels for data time-locked with movement and with the visual cues. Then we used MCE in the frequency domain to find out what brain areas were coherent with somatomotor cortex.



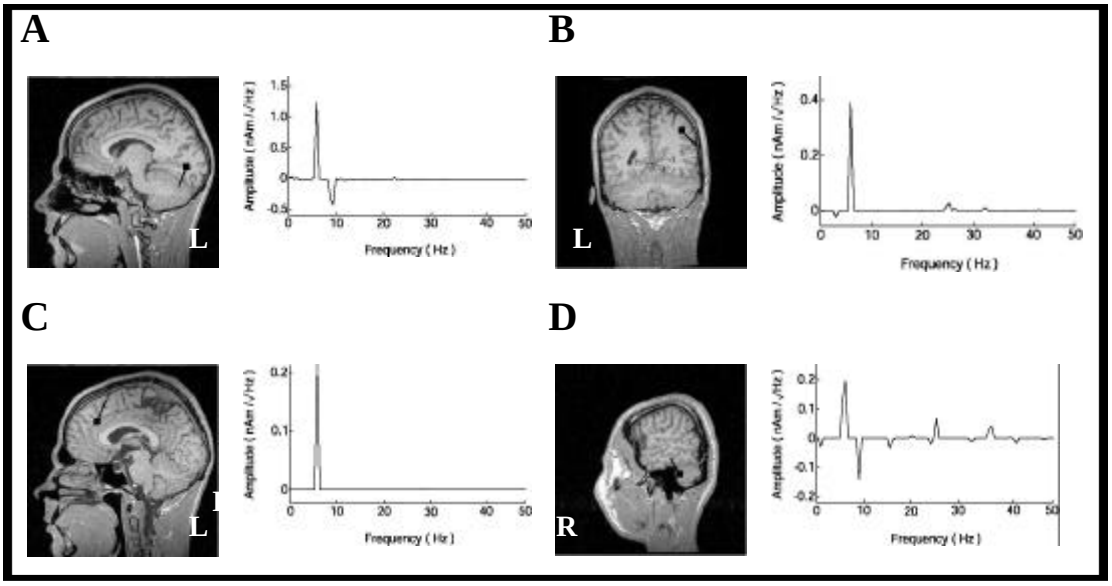
This is a snapshot of which brain areas are oscillating coherently and in phase with the left somatomotor cortex at 5.8 Hz during processing of the 2nd cue.

This is a snapshot of which brain areas are oscillating coherently and in phase with left somatomotor cortex at 5.8 Hz during processing of the 4th + 6th cues.

This is a snapshot of which brain areas are oscillating coherently and in phase with left somatomotor cortex at 5.8 Hz during processing of the 4th – 6th movements.

The images A and B demonstrate that the dynamic shift in the location of the activated brain areas observed in the time-domain data is mirrored in strong differences also in the frequency domain as this subject learns to produce anticipatory movement. Interestingly, the rather striking

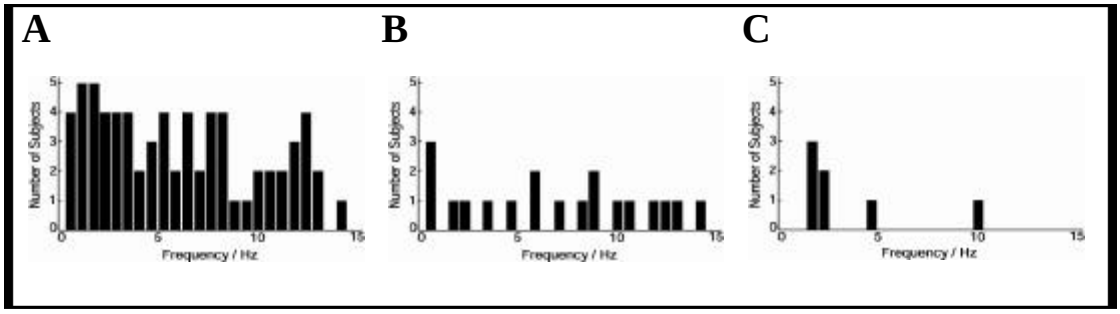
similarities between the MCE images B and C, for activity time-locked with cue presentation and movement respectively, in these coherence data no longer reflect the similarities seen in the corresponding time-domain data.



We used the MCE inversion again in the frequency domain to identify current dipole approximates for VOAs undergoing coherent oscillations in phase with somatomotor cortex at 5.8 Hz. A coherence network was extracted from event-related averages time-locked with presentation of the 4^{th} + 6^{th} visual cues that included, A) the left extrastriate visual cortex, B) right parietal cortex, C) right anterior cingulate cortex, and D) right lateral cerebellum.

These data demonstrate that the left somatomotor cortex undergoes coherent oscillation at 5.8 Hz with both the right lateral cerebellum and areas associated with processing of visual stimuli. These seemingly disparate sensory and motor areas are not just active during the same epoch, as was noticed in the time-domain data, but, remarkably, contain neuronal populations that oscillate at a common frequency and are phase-locked with the presented stimuli.

Do cortico-cerebellar networks show evidence of plastic change during the development of anticipatory movement? We looked for changes at each frequency interval of the locations of sources in the cerebellum that were coherent with contralateral somatomotor cortex.



The bar graphs above show the number of subjects with sources in cerebellum, pons and inferior olive that were coherent with contralateral somatomotor cortex as a function of frequency: A) sources unique to the 2^{nd} cue, B) sources unique to the 4^{th} + 6^{th} cues, and C) sources common to both the 2^{nd} and 4^{th} + 6^{th} cues.

Thus, the coherence networks that are active when the subjects are just beginning to predict the future are different from the networks that are active when they have really "got the hang of it." This strongly suggests that these shared cortico-cerebellar oscillations really do reflect short-term learning. Even the frequency of these oscillations makes sense, with many of the sources oscillating in a 6-12 Hz bandwidth that is characteristic of "error messages" presumed to originate in the inferior olive.

Summary

What have we learned from this study? First, we have an exquisitely sensitive tool for detecting interactions between different brain areas in normal human subjects. We have an analysis method that allows us to parse brain activity into networks based on phase-locked coherent oscillatory activity. This is very important. The brain is immensely complex. We must have some way of simplifying our description of brain activity, something comparable to a set of "basis states" or a "periodic table." The elements cannot be just static locations or connections, but must represent dynamic, transient, functional couplings.

A growing group of neuroscientists have used both non-invasive and invasive methods to identify coherence networks that link cortical areas, particularly during perception of complex visual input. We have used cued movement to discover that the cerebellum also can be part of transient coherence networks. This links the cerebellar half of the human brain with the cortex in mutual oscillatory behavior.

What is the program for the future? We plan to use MEG / MCE coherence analysis to characterize network phenomena in the human brain. We are interested in identifying plastic changes in these networks that may correlate with learning and memory processes and, importantly, may be used to predict behavior. We anticipate that these and similar methods will be used to study a wide range of sensory, motor and cognitive functions in both the normal and abnormal brain.

I have discussed for the most part application of MEG in basic research through the use of a representative study. MEG provides detailed information on the dynamics of brain function. We began with the hypothesis that human behavior is the product of ongoing processes in the brain and is thus constrained by and emerges from the structure, connectivity and function of distributed brain areas. We have access with MEG not just to superficial cortical areas, but also to deep brain structures crucial to memory and learning, to the hippocampus, the amygdala and also to the cerebellum. There is an ongoing program to use MEG to investigate a wide variety of brain dysfunction, including epilepsy and schizophrenia. Importantly, MEG may have the potential to observe subtle, developing abnormalities in brain function even before they are manifest in behavioral deficits.

Final Comments: MEG in Space?

What might be the possible applications of a whole-scalp MEG array that might be of interest to NASA? An example of an earth-based study would be to investigate how brain functions that involve the cerebellum are changed by prolonged space flight. The cerebellar cortex is very self-similar and highly interconnected. Does cerebellar plasticity induced by adjusting all motor programs to accommodate a low gravity or gravity-free environment impact other, more cognitive functions of human cerebellum? For example, cortico-cerebellar circuits are known to be essential for a fundamental form of learning, classical "delay" conditioning. Can we use MEG to scan brain function for subtle, developing deficits in cognition, even before overt differences in behavior are detected?

What about a space-based array? The engineering challenges that must be met to provide such a capability are considerable, and they include either the use of DC SQUIDs and their burden for a cryogenic environment or an alternative magnetic field sensor. Optically pumped magnetometers may be very interesting in this regard. However, even if the need for a cryogenic environment is eliminated, the tremendous effort by the MEG community to develop both hardware and software methods to reduce the effects of ambient magnetic field fluctuations, compensate for subject movement, implement artifact rejection and utilize a wide variety of data analysis algorithms for data interpretation should prove invaluable irrespective of the type of sensors envisioned.

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Role of Fundamental Physics in Human Space Exploration

Slava Turyshev
Jet Propulsion Laboratory, California Institute of Technology

This talk will discuss the critical role that fundamental physics research plays for the human space exploration. In particular, the currently available technologies can already provide significant radiation reduction, minimize bone loss, increase crew productivity and, thus, uniquely contribute to overall mission success. I will discuss how fundamental physics research and emerging technologies may not only further reduce the risks of space travel, but also increase the crew mobility, enhance safety and increase the value of space exploration in the near future.

The work described here was carried out at the Jet Propulsion Laboratory, California Institute of Technology under a contract with the National Aeronautic and Space Administration.

Ultra-sensitive non-cryogenic magnetometer for space missions

Michael Romalis
Princeton University

Ultra-sensitive magnetic field measurements have long relied on SQUID magnetometers cooled by LHe or LN2. Our group recently developed a non-cryogenic atomic magnetometer that rivals the sensitivity of the best SQUID magnetometers. The device uses optically-pumped K vapor and detects the precession of the K electron spins in the magnetic field. A key factor in achieving high magnetic-field sensitivity is suppression of spin-exchange relaxation due to collisions between alkali-metal atoms, which is normally the dominant source of magnetic resonance broadening. Using the spin-exchange relaxation-free (SERF) atomic magnetometer we demonstrated magnetic field sensitivity as low as 0.5 $fT/Hz^{1/2}$ and suppression of external magnetic-field noise with a multi-channel gradiometer. A fT-level multichannel non-cryogenic magnetometer can find a number of applications on space missions. It will allow non-contact remote sensing of magnetic fields produced by the heart and the brain and could be used for continuous monitoring of astronaut's heart rhythms and of brain activity during sleep and in demanding mental tasks. Electrical measurements of this type have been widely used for health monitoring but require either electrical contact or proximity of the sensors. A fT-level magnetometer will also allow detailed studies of remnant rock magnetization on the Moon and Mars.